

Remarks/Arguments

Applicant wishes to thank the Examiner for the courtesy of an interview on July 22, 2003, attended in person by the Examiner and Applicant/Inventor Dr. Babak Nemat and joined by Jean Ellis, J.D., an associate attorney for Applicant, via telephone. The Examiner's comments in clarifying the rejections set forth in the present Office Action were most helpful and greatly assisted Applicant in preparation of the present response.

The claim amendments are submitted to put the claims in better form for allowance and/or in better form for consideration on appeal, and were made after considering points raised by the Examiner during the interview. The 132 Declaration is submitted to support these claim amendments, as well as for the purpose of overcoming new grounds of rejection made in Final Office Action. Reconsideration and entry of the amendment is respectfully requested.

In the Specification

By the present amendment, Applicant has amended the title of the application to more particularly describe the presently claimed invention, which is directed to an apparatus to enhance optical transparency of biological tissue.

In the Claims

Claims 37-69 were pending prior to this response. By the present communication, claim 37 has been amended to define Applicant's invention with greater particularity and to put them in better condition for allowance Claim 70 has been added as a specific embodiment of the invention. The amendments add no new matter, being fully supported by the Specification and original claims:

Amendment to claim 37 to specify "porative means" finds support throughout the Specification, including at page 19, second paragraph.

Amendment to claim 37 to specify “with minimal tissue damage” is supported throughout the Specification, including at page 5, first paragraph.

Amendment to claim 37 to specify that the clarifying agent is delivered to the surface of the tissue permeability barrier “for delivery therethrough” is supported throughout the Specification, including page 15, second paragraph.

Amendment to claim 37 to specify that the clarifying agent is locally delivered to the target biological tissue is supported throughout the Specification by reference to delivery to target tissue and at page 5, first paragraph, where “local delivery” is inferred by avoidance of collateral, or non-local, tissue.

Amendment to claim 37 to specify “interstitial space” is supported throughout the Specification, including at page 15, first paragraph.

Amendment to claim 37 to specify “wherein said porative means and said delivery means are operated simultaneously or sequentially to deliver the clarifying agent to the interstitial space of the target tissue to transiently enhance the transparency thereof” is supported throughout the Specification, including at page 19 and Figure 6. For instance, when the porative means is electroporation, the nature of the process permits an ordering of events such that the clarifying agent is delivered to the surface permeability barrier simultaneous with poration of the surface permeability barrier by electroporation, or the two events can occur sequentially, e.g., the clarifying agent is delivered to the surface permeability barrier either before or after electroporation thereof. When chemical enhancement of trans-membrane delivery is the porative means, then, likewise, the clarifying agent can be delivered to the tissue permeability barrier simultaneously with chemical enhancement, or delivery and poration can be sequential.

Amendment of claim 37 to specify that “said light means is operational thereafter for light delivery to, or detection from, the target tissue” is supported throughout the Specification, including the Examples, which exemplify that the porative and delivery

means are operational before the light means is operational, such that the clarifying agent effects transparency of the target tissue prior to operating the light means for light delivery to, or detection from, the tissue.

New claim 70 finds support throughout the Specification, including at page 19, second paragraph.

Accordingly, claims 37-70 are currently pending in the application.

The Rejection under 35 U.S.C. §102(b)

Claims 37-56, 62, and 69 are rejected under 35 U.S.C. §102(b) as being anticipated by Martinez (US 4,222,375). Martinez discloses an apparatus alleged to be capable of enhancing the optical transparency of biological tissue comprising means for bypassing the surface barrier (needle), means for delivering clarifying agent (syringe), means for delivery of light (fiber optic cable). The Examiner asserts that the various uses recited in the claims are readable on the prior art because the prior art is capable of performing these functions and supplying light for these functions.

Applicant respectfully disagrees with the Examiner's position. The Martinez apparatus is designed to illuminate internal tissue before and during a medical procedure. In essence, it comprises a cannula and a light source. In one embodiment, the Martinez apparatus also comprises a syringe to serve as a reservoir for either delivery of a drug to an internal body site or receipt of fluid removed from an internal body site. Martinez has no disclosure or suggestion that the disclosed apparatus is capable of bypassing a tissue permeability barrier, such as stratum corneum or conjunctiva of the eye, or that the disclosed apparatus can be used to deliver a clarifying agent to a target tissue to transiently enhance the transparency thereof. Moreover, there is no disclosure or suggestion that the Martinez apparatus can bypass a tissue permeability barrier with minimal tissue damage, as is recited in the present claims.

More particularly, and as recited in claim 37, Martinez does not disclose an apparatus comprising (a) a porative means for bypassing said surface permeability barrier of tissue to deliver agent to the interstitial space, (b) with minimal tissue damage to permit the delivery of a clarifying agent past said surface permeability barrier. At best, Martinez discloses that a hypodermic needle that is cut and bored to have an aperature and opening on its side for fluid delivery or aspiration, can be used with the cannula to deliver or collect fluid (Martinez '375, col. 4, lines 31-32). There is no teaching or suggestion in Martinez that such a needle, or any other element of the Martinez apparatus, is a porative means for bypassing the surface permeability barrier of tissue such that it can deliver clarifying agent to the interstitial space.

Further, Martinez expressly states that a tissue incision is required when the cannula/light device is used to deliver or aspirate fluid (Martinez, col. 4, lines 13-18). Again, this is in contrast to the apparatus of present claim 37, which bypasses the surface permeability barrier with only minimal tissue damage such that the anatomical integrity of the target tissue and collateral tissue is maintained, and the clarifying agent is delivered precisely to the target interstitial space. This difference between the apparatus disclosed by Martinez and the apparatus of claim 37 further distinguishes the Martinez apparatus from the claimed apparatus.

Applicant has provided a Declaration under 37 C.F.R. §1.132, attached hereto as Appendix I, and incorporated herein, to state his opinion that the apparatus disclosed by Martinez does not include an element to bypass the tissue permeability barrier with minimal tissue damage. Applicant also states his opinion that the Martinez apparatus cannot perform the functions of the presently claimed apparatus, because it would result in more than minimal tissue damage.

It is for these reasons that Martinez cannot support a rejection of claims 37-56, 62, and 69 under 35 U.S.C. §102(b). Applicant respectfully requests reconsideration and removal of the rejection.

The Rejection under 35 U.S.C. §103(a)

Chan et al.

Claims 37-52, 54-56, 62-64, 66 and 69 are rejected under 35 U.S.C. §103(a) as allegedly being obvious in view of Chan et al. (US 6,275,726; "Chan"). Chan is said to disclose a means for bypassing the surface permeability barrier of tissue, means for delivering a clarifying agent, and means of light delivery for diagnostic and therapeutic applications. The Examiner asserts the various skin appendages will inherently be affected when the agent is injected into the tissue. While the Examiner concedes that Chan does not disclose the various parts to be used in one apparatus, the Examiner asserts that it is well within the knowledge of the skilled artisan to make that which comprises plural parts into one part to simplify use of a device. The mere combining of the apparatus without a more specific recitation of the structural relationship between the parts is alleged to be obvious to one of ordinary skill in the art.

Applicant respectfully asserts that the presently claimed apparatus is not obvious in light of the Chan disclosure. First, Chan makes no suggestion or hint that the separate elements of (a) a means for bypassing a surface permeability membrane with minimal tissue damage, (b) a means for delivering a clarifying agent to the surface permeability membrane, and (c) a light source for light delivery to, or detection from, the target tissue could be assembled into a single device, or that such assembly would make operation simpler. Instead, parts (a) and (b) are generally discussed by Chan as separate elements, and Chan always refers to the light source (c) as separate from parts (a) and (b).

Second, it is well understood that the mere fact that a reference can be modified to reach the claimed invention is insufficient to establish prima facie obviousness; there must be an additional objective basis upon which to support the rejection. Here, the applications disclosed by Chan for its method are varied, e.g., treatment of port wine stains and spider veins, photodynamic therapy, interstitial photocoagulation, hair removal, fluorescence spectroscopy, visual diagnostics, blood glucose monitoring, tissue imaging (Chan '726, col. 7, line 36 through col. 8, lines 65). Light sources for each of

these diverse applications also are varied, and have been developed and tailored to the specific applications. The level of diversity in applications, light sources, and operators (e.g., physicians, technicians, etc.) argue against the Examiner's position that one of ordinary skill would make the combination to simplify the apparatus, as one of ordinary skill would lack the knowledge to understand which elements, and how, to assemble the claimed apparatus.

Thus, Chan provides insufficient basis to conclude that the concept of combining, in a single device, (a) a means for bypassing a surface permeability membrane, (b) a means for delivering a clarifying agent to the surface permeability membrane, and (c) a light source for light delivery to, or detection from, the target tissue, would be a simple next step or design choice.

Moreover, claim 37 has been amended to recite an operational relationship among the three elements, such that said porative means and said delivery means are operated simultaneously or sequentially to deliver the clarifying agent to the interstitial space of the target tissue to transiently enhance the transparency thereof, and said light means is operational thereafter to permit light delivery to, or detection from, the target tissue. Such a relationship is not disclosed by Chan and is not trivial, in that the time sequence in which the porative and delivery means are operated has a significant impact on the tissue transparency effect achieved.

Attached hereto as Appendix I is a Declaration of Applicant/Inventor supporting the positions stated above, and his opinion that one of ordinary skill in the relevant art would not have had the requisite insight or knowledge to combine the separate elements of Chan into a single apparatus. It was the special expertise of the present inventor, which crosses several art field, that led to his recognizing and making the invention. Further, it is also the opinion of the Applicant/inventor that the operational relationship among the elements of the presently claimed apparatus is not trivial and would not have been obvious to one having ordinary skill in the art. Thus, the Declaration in Appendix I provides his opinion that it would not have been obvious to one of ordinary skill in the art

to combine the separate elements disclosed by Chan into a single apparatus as presently claimed.

While the above comments are directed to claim 37, they apply as well to claims 38-52, 54-56, 62-64, 66, and 69, which depend from claim 37. For the reasons set forth herein, Applicant respectfully requests reconsideration and removal of the rejection under 35 U.S.C. §103(a) in view of Chan.

The Rejection under 35 U.S.C. §103(a)

Martinez , in view of Edwards and Weaver, respectively

Claims 53, 57-59, 61, 65 and 67 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Martinez as applied to claims 37 and 38 above, and further in view of Edwards (US 5,833,647; "Edwards"). Martinez is said to disclose the claimed invention except for a bypassing means including iontophoresis system, electric pulse generator, acoustic generator, and temperature gradient. Edwards teaches using these methods, which inherently require the appropriate systems and generators to drive molecules. The Examiner alleges it would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Edwards in the invention of Martinez in order to deliver the agent across the skin barrier.

Claims 60 and 68 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Martinez as applied to claim 37 above, and further in view of Weaver (US 5,019,034; "Weaver"). Martinez is said to disclose the claimed invention except for a bypassing means to apply optical pressure and penetrating solvent. Weaver teaches the use of means to apply optical pressure and penetrating solvent for transdermal delivery. The Examiner alleges it would have been obvious to one of ordinary skill in the art at the time of the invention to facilitate delivery of an agent across the skin barrier.

Claims 53, 57-59, 60, 61, 65, 67, 68, rejected under 35 U.S.C. §103(a), are dependent on claim 37, which is not subject to the present rejection. It is well established

that a dependent claim cannot be found to be obvious if the claim from which it depends is not found to be obvious. Therefore, because claim 37 is not rejected, and the rejected claims depend from claim 37, the rejection of claims 53, 57-59, 60, 61, 65, 67, and 68 over Martinez in view of Edwards and Weaver, respectively, is improper.

Nevertheless, even if claim 37 were included in the present rejection, there is insufficient support for rejection of claim 37, and claims 53, 57-59, 60, 61, 65, 67, and 68 dependent therefrom, over Martinez in view of Edwards and Weaver. As noted in the discussion of Martinez under the 35 U.S.C. §102(b) rejection, the Martinez apparatus is concerned with supplying a direct light source to an internal body site during a medical procedure. The Edwards disclosure is directed to a method of enhancing transport of a therapeutic drug, i.e., vasopressin, calcein, insulin, from a drug-containing hydrogel or lipogel that serves as a carrier for the drug during transdermal delivery. The Examiner has not provided any basis upon which one of ordinary skill in the relevant art would have had the requisite motivation to combine the Martinez internal tissue illumination device with the Edwards transdermal method of transporting a drug from a hydrogel to skin, in order to define the apparatus of claim 37 for transiently enhancing the transparency of a target tissue. Applicant strongly asserts that Martinez and Edwards are nonanalogous art directed to solving two different problems: illuminating an internal tissue during a surgical procedure (Martinez) and transporting a drug from a hydrogel to the external side of skin (Edwards). It is for these reasons that one of skill would not have been motivated to combine Martinez and Edwards in the manner suggested by the Examiner.

Furthermore, even if one did combine the Martinez disclosure with the Edwards disclosure, the combination would not define each and every element of present claim 37. For instance, the porative means in element (a) of claim 37 is not taught by either reference separately or in combination. (For the sake of brevity, each and every difference between claim 37 and the combined disclosures of Martinez and Edwards is not listed here.)

Similarly, the Examiner has not indicated why one of skill in the relevant art would be motivated to combine the Martinez disclosure with the Weaver disclosure to define the invention of claim 37. The differences between the nonanalogous arts of Martinez (lighting for internal surgery) and Weaver (transdermal delivery) and the differences between the problem each attempts to solve, would not suggest that the references could be combined to reach the apparatus of claim 37, whose purpose is to enhance tissue transparency. Moreover, even if the combination was made, the combined disclosure does not define each and every element of claim 37. Like Martinez and Edwards, the Martinez and Weaver combination also fails to disclose a porative means. (For the sake of brevity, each and every difference between claim 37 and the combined disclosures of Martinez and Weaver is not listed here.)

Therefore, absent any motivation for one of ordinary skill in this art to combine Martinez and Edwards or Martinez and Weaver, and the fact that even if the combinations were made they would not define each and every element of the claim 37 apparatus, claim 37 cannot be found obvious in light of these references. Because claim 37 is patentable in light of Martinez and Edwards, so, too, are claims 53, 57-59, 61, 65 and 67, which depend from claim 37.

Applicant respectfully requests reconsideration and removal of the rejection under 35 U.S.C. §103(a).

Request for an Interview

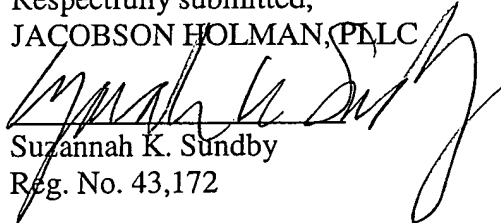
Should there be any remaining issues after entry of the amendment and consideration of the remarks herein, Applicant respectfully request either an in-person interview or a telephonic interview with the Examiner.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. **06-1358**, referencing Attorney Docket No. **P66960US2**.

Respectfully submitted,
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